



DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

18 MAY 2016

MEMORANDUM FOR SGOED

ATTN: MAJ JOSEPH MADDRY

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Comparison of Hydroxocobalamin Versus Norepinephrine Versus Saline in a Swine Model of Severe Septic Shock** presented at/published to the **Lightning Oral, SAEM Conference, New Orleans, LA 10-13 May 2016** with MDWI 41-108, and has been assigned local file #16200.
2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.
3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.
4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
 - a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]
 - b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.
2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.
3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.
4. Attach a copy of your abstract, paper, poster and other supporting documentation.
5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.
6. On page 2, have either your unit commander, program director or immediate supervisor:
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7. Submit your completed form and all supporting documentation to the CRD for processing (59crdpubspres@us.af.mil). If you have any questions or concerns, please contact the 59 CRD/ Publications and Presentations Section at 292-7141 for assistance.
8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.
9. Once your manuscript, poster or presentation has been approved for a one-time public release, you may proceed with your publication or presentation submission activities, as stated on this form. **Note:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.
10. If your manuscript is accepted for scientific publication, please contact the 59 CRD/Publications and Presentations Section at 292-7141. This information is reported to the 59 MDW/CC. All medical research or technical information publications/presentations must be reported to the Defense Technical Information Center (DITC). See 59 MDWI 41-108, *Presentation and Publication of Medical and Technical Papers*, for additional information.

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:

"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving humans:

"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."

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"The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS			
1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol) Joseph Maddry / Maj / O-4 / SGOED	3. GME/GHSE STUDENT: <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO	4. PROTOCOL NUMBER: FWH20130033A
5. PROTOCOL TITLE: (NOTE: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.) Cobalamin as a treatment for battle associated severe sepsis-induced shock in swine (Sus Scrofa)			
6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED: Comparison of hydroxocobalamin versus norepinephrine versus saline in a Swine model of severe septic shock			
7. FUNDING RECEIVED FOR THIS STUDY? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO FUNDING SOURCE: AFMSA			
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13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email) Maddry, Joseph K. joseph.k.maddry.mil@mail.mil			14. DUTY PHONE/PAGER NUMBER 210-630-7374
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I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.			
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Comparison of hydroxocobalamin versus norepinephrine versus saline in a swine model of severe septic shock.

Background: Sepsis is associated with a mortality of nearly 30%. Mortality is due, in part, to an uncontrolled inflammatory response. Matrix metalloproteinase-9 (MMP-9) and heat shock protein 70 (HSP 70) have been suggested to be biomarkers of severe sepsis and may be useful indicators of treatment success. Hydroxocobalamin (HOC), which regulates inducible nitric oxide synthase and increases systemic vascular resistance, may be effective in treating sepsis-induced hypotension and reversing overexpression of inducible nitric oxide synthase.

Objective: To compare efficacy of HOC versus norepinephrine (NOR) versus saline in swine with lipopolysaccharide (LPS)-induced endotoxemia.

Methods: Swine (45-55 kg) were anesthetized, intubated, and instrumented with continuous femoral and pulmonary artery pressure monitoring. Endotoxemic shock, defined as a 50% decrease in mean arterial pressure (MAP) compared to baseline, was established with a two hour escalating infusion of LPS (5-60 mcg/kg/hr) followed by a continuous infusion of LPS (20 mcg/kg/hr). MAP remained at 50% of baseline for one hour before treatment ensued. Animals received either 200 mg/kg bolus of HOC followed by a maintenance infusion of 15 mg/kg, NOR infusion titrated to maximize MAP and maintain HR \leq 180 BPM, or saline (1.5 mg/kg/hr). A sample size of 10 animals per group was determined based on a power of 80% and an alpha of 0.05 to detect a difference between groups using repeated measures MANOVA.

Results: We previously reported that HOC and NOR were comparable in supporting MAP and significantly better than saline ($p < 0.01$). We now report whereas MMP-9 or HSP 70 values were not significantly different at baseline between groups ($p = 0.4$; 0.13), nor was there a difference between groups after two hours of LPS infusion ($p = 0.5$ and 0.3), there was a significant within group difference such that LPS increased MMP-9 and HSP 70 over time ($p < 0.01$; < 0.01) prior to treatment. After treatment MMP-9 values fell significantly in the HOC group compared to the other groups ($p < 0.02$) and HSP 70 decreased in the HOC and NOR groups compared to saline treatment ($p < 0.05$)

Conclusions: An infusion of intravenous HOC appears to be comparable to NOR in decreasing biomarkers associated with severe LPS-induced endotoxemic shock and significantly better compared to saline in our experimental animal model.